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Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended). A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, said non-hemolytic cytolytic peptide being selected from the group consisting of:

- (A) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising only D-amino acid residues, and comprising an α -helix breaker moiety;
- (B) a non-natural synthetic peptide comprising both L-amino acid residues and D-amino acid residues (i) composed of a

ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid, (ii) having a net positive charge which is greater than +1, (iii) having a ratio of hydrophobic to positively charged amino acids such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells, and (iv) having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature, and cyclic derivatives thereof; and

- (C) a random copolymer consisting of a hydrophobic, a positively charged and a D-amino acid; with the proviso that the peptide is not that of SEQ ID NO:1, SEQ ID NO: 12, SEQ ID NO: 14 or SEQ ID NO:23.

2. (Currently Amended). A cyclic non-hemolytic cytolytic peptide according to claim 1(A) having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic

effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, wherein said non-hemolytic cytolytic peptide is a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising only D-amino acid residues, and comprising an α -helix breaker moiety.

3. (Original) The cyclic peptide according to claim 2, which is a cyclic diastereomer derived from pardaxin or mellitin or from fragments thereof.

4. (Original) The cyclic peptide according to claim 3, in which the net positive charge greater than +1 is due to the native amino acid composition, or is attained by neutralization of free carboxyl groups or by the addition of positively charged amino acid residues and/or positively charged chemical groups.

5. (Original) The cyclic peptide according to claim 4, which is selected from a cyclic diastereomer of pardaxin or of a fragment thereof to which Lys residues have been added to

the N-terminus and/or aminoethylamino groups have been added to the C-terminus.

6 (Currently Amended). A cyclic peptide according to claim \pm 2, selected from the group of cyclic pardaxin-derived peptides consisting of the herein designated peptides 86-88 (SEQ ID NOS: 86-88, respectively), of the sequence:

86) Cyclic $K^1[D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys,

87) Cyclic $K^1 K^2[D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys, and

88) Cyclic $K^1 K^2K^3 [D]P^7 L^{18}L^{19}$ [1-22]-par of the sequence:

Cys-Lys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-
Ser-Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys.

Claim 7 (Cancelled).

8. (Currently Amended). The A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-

naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, said non-hemolytic cytolytic peptide according to
~~claim 7,~~ having the following characteristics: ~~(a)~~ (i) it is a non-natural synthetic peptide composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid, ~~(b)~~ (ii) the peptide has a net positive charge which is greater than +1, ~~(c)~~ (iii) the ratio of hydrophobic to positively charged amino acids is such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells, and (iv) having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature, and cyclic derivatives thereof.

9. (Previously Amended). The peptide according to claim 8, wherein the positively charged amino acid is selected from the group consisting of lysine, arginine and histidine,

and the hydrophobic amino acid is selected from the group consisting of leucine, isoleucine, glycine, alanine, valine, phenylalanine, proline, tyrosine and tryptophan.

10. (Previously Presented). The peptide according to claim 9, wherein the net positive charge greater than +1 is due to the amino acid composition or to the addition of positively charged chemical groups, or which hydrophobicity is decreased by the addition of polar amino acids selected from the group consisting of serine, threonine, methionine, asparagine, glutamine and cysteine.

11. (Previously Presented). The peptide according to claim 10, having at least 6 amino acid residues, in which the hydrophobic amino acid is leucine, alanine or valine, and the positively charged amino acid is lysine.

12. (Currently Amended). The A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood

cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, wherein:

said non-hemolytic cytolytic peptide is (i) composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid, (ii) the peptide has a net positive charge which is greater than +1, (iii) having a ratio of hydrophobic to positively charged amino acids such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells, and (iv) having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature, and cyclic derivatives thereof;

the positively charged amino acid is lysine and the hydrophobic amino acid is leucine; and

said non-hemolytic cytolytic peptide is being a
diastereomer of a 6-mer, 8-mer or 12-mer peptide composed of leucine and lysine, in which at least one third of the sequence is composed of D-amino acids, but excepting the peptide herein designated 23 (SEQ ID NO:23):

23) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂.

13. (Previously presented). A Leu/Lys diastereomer according to claim 12, selected from the group of peptides consisting of those herein designated 24 to 29 (SEQ ID NO:24-29, respectively), of the sequence:

24) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,

25) Lys-Lys-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Lys-Lys-NH₂,

26) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂,

27) Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-NH₂,

28) Lys-Leu-Leu-Leu-Leu-Lys, and

29) Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys.

14. (Currently Amended). A cyclic derivative of a non-natural non-hemolytic cytolytic synthetic peptide ~~according to claim 7~~ having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in

which it manifests said cytolytic activity on pathogenic cells, wherein:

said non-hemolytic cytolytic peptide is (i) composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid, (ii) the peptide has a net positive charge which is greater than +1, and (iii) having a ratio of hydrophobic to positively charged amino acids such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells; and (iv) having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature;

the net positive charge greater than +1 is due to the amino acid composition or to the addition of positively charged chemical groups, or which hydrophobicity is decreased by the addition of polar amino acids selected from the group consisting of serine, threonine, methionine, asparagine, glutamine and cysteine;

said non-hemolytic cytolytic peptide has at least 6 amino acid residues, in which the hydrophobic amino acid is leucine and the positively charged amino acid is lysine; and

said non-hemolytic cytolytic cyclic peptide is selected from the group of peptides consisting of those herein designated 92-95 (SEQ ID NOS:92-95,respectively), of the sequence:

92) Cyclic Cys Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys Cys,
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93) Cyclic Cys Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Lys Cys,
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94) HN - Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys - CO, and
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95) HN - Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys - CO.
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Claims 15-19 (Cancelled)

20. (Currently Amended). A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity

Appln. No. 09/367,714
Amd. dated January 12, 2004
Reply to Office Action of September 12, 2003

on pathogenic cells, said non-hemolytic cytolytic peptide
being a random copolymer according to claim 1(C) consisting of
a hydrophobic, a positively charged and a D-amino acid.

21. (Previously Amended). The non-hemolytic
cytolytic random copolymer according to claim 20, consisting
of lysine, leucine and D-leucine in the ratio 1:1:1, 2:1:1 or
3:1:1 (Mol).

Claims 22-26 (Cancelled)

27. (Currently Amended). A The composition
according to claim 38, for use in the treatment of infections
caused by pathogenic organisms comprising an acceptable
carrier and a peptide according to claim 1 in an amount
effective to inhibit bacterial growth .

28. (Currently Amended)-A The composition according
to claim 27, wherein the pathogenic organism is selected from
the group consisting of bacteria, fungi, protozoa and
mycoplasma comprising an acceptable carrier and a peptide
according to claim 1 in an amount effective to inhibit growth
of fungi .

29. (Currently Amended). A The composition according to claim 38, for use in the treatment of cancer comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit proliferation of cancer cells.

Claims 30-34. (Cancelled).

35. (Currently Amended). The mixture of claim 34 39, wherein each peptide or derivative present in the mixture consists of 12 amino acids, each of which is selected from the group consisting of L-Leu, D-Leu, L-Lys, and D-Lys.

Claim 36 (Cancelled)

37. (Previously Presented). The mixture according to claim ~~35~~ 39, comprising a mixture of Lys/Leu 12-mer peptide diastereomers.

38. (new). A composition comprising a pharmaceutically acceptable carrier and a non-hemolytic cytolytic peptide according to claim 1.

39 (New). A mixture consisting of two or more non-hemolytic cytolytic peptides or cyclic derivatives thereof,

Appln. No. 09/367,714

Amd. dated January 12, 2004

Reply to Office Action of September 12, 2003

said peptides having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity on pathogenic cells, each said non-hemolytic cytolytic peptide being a non-natural synthetic peptide (i) composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid, (ii) having a net positive charge which is greater than +1, (iii) having a ratio of hydrophobic to positively charged amino acids such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells, and (iv) having a sequence of amino acids such that the same amino acid sequence in which each residue is in the L-configuration is not found in nature.